Appendix S4. Secondary outcomes

Three studies investigated preterm birth at earlier gestational age thresholds (Table S9 and Table S10).[1–3] Two studies[1,2] reported adjusted odds ratios from these analyses that were higher in magnitude than their conventional preterm birth analyses (based on the cut-off of <37 weeks). Mean gestational age comparisons were reported by six studies (Table S11). Apart from one study that reported an unadjusted mean difference of one full week between women who had 2009 pandemic H1N1 influenza disease during pregnancy compared with those who did not (mean gestational age 37.3 weeks and 38.3 weeks, respectively; *P*-value <0.001),[1] mean differences reported by other studies were small (between 0.1 and 0.3 weeks) and not statistically significant.

Ten of 12 estimates for low birth weight (<2,500 grams) had confidence intervals that included the null value (point estimates ranged from 0.40 to 1.48) (Table S12). Two studies from the 2009 H1N1 pandemic report statistically significant odds ratios greater than one (adjusted ORs ranged from 1.67 to 3.2);[1,2] however, neither accounted for gestational age in the analysis of low birth weight, despite a higher risk of preterm birth among women with influenza illness (approximately 24% among women with pandemic H1N1 illness in both studies).[1,2] One study reported that a significant birth weight reduction (by -255 grams) among women with severe pandemic 2009 H1N1 illness, compared with women from the general obstetrical population, disappeared following adjustment for gestational age.[2] In contrast, two other studies from the 2009 pandemic reported no association between maternal influenza disease and low birth weight, but both ascertained a lower severity of maternal influenza illness and both accounted for gestational age in their analyses.[4,5] No difference in the proportion of low birth weight infants between the active treatment and placebo groups was observed in the RCT.[6]

The results from 13 studies that reported continuous birth weight are challenging to interpret, owing to inconsistent reporting of absolute differences and variance measures, both of which were computed by review authors where possible (Table S13). Of four studies that accounted for gestational age either through restriction to term births or matching on gestational age, two reported a higher mean birth weight[7,8] and two a lower mean birth weight[9,10] among infants born to women with influenza illness or infection during pregnancy compared with no influenza (mean difference ranged from -99 grams to 70 grams; Table S13). Among studies that did not account for gestational age in any way, both reductions and increases in birth weight were reported. The median birth weight did not differ between randomized treatment groups in the RCT.[6]

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